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Running head: *Developing a Hybrid CBT and ACT Intervention for MS Pain*

# **Using mixed methods case-series evaluation in the development of a guided self-management hybrid CBT and ACT intervention for Multiple Sclerosis pain.**

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## **Abstract**

**Purpose:** Two-thirds of people with Multiple Sclerosis (pwMS) experience pain. Medications provide minimal relief, and current non-pharmacological interventions lack a clear conceptualisation of MS pain. This study explored the potential efficacy of a telephone-supported hybrid CBT and ACT self-management intervention for pwMS based on an empirically supported model of MS pain using a replicated single-case series design.

**Methods:** Seven pwMS with varied demographic and disease characteristics completed the 8-week home-based programme alongside 3 hours of telephone support. Online questionnaires were completed every four days for 16 weeks (4-weeks baseline, 8-weeks treatment, 4-weeks follow-up). The primary outcomes were pain severity and interference. Psychological process variables drawn from the MS pain model were also completed, and post-treatment qualitative interviews conducted.

**Results:** Simulation Modelling Analysis (SMA) showed three patients had large improvements in pain outcomes, two showed no change, and two worsened. Five participants showed significant change on various psychological process variables. Change in pain catastrophizing was the most consistent finding.

**Conclusions:** Findings suggest a self-management programme for MS pain with minimal therapy support may be effective for some pwMS, but not those with more complex comorbidities. Participants suggested web-based delivery may simplify the approach, and therapist telephone contact was highly valued.

**Key words:** Multiple sclerosis; pain; cognitive behaviour therapy (CBT); acceptance and commitment therapy (ACT); case series; longitudinal study.

## Introduction

Multiple Sclerosis (MS) is a chronic disease of the central nervous system affecting around 2.1 million people worldwide [1]. The majority of people with MS (pwMS) are diagnosed with relapsing remitting disease (RRMS), which includes periods of partial or total remission where the disease is inactive, interspersed with symptom relapses. Many pwMS go on to develop chronic secondary-progressive illness (SPMS), where impairment accumulates over time (Murray, 2006), whilst a minority experience a chronic-progressive worsening of symptoms and disability from onset, known as primary-progressive MS (PPMS) [2]. Around 63% of people with MS (pwMS) are affected by pain [3]. MS pain can be acute or chronic. It is broadly classified as either neuropathic, arising from damage to nerve fibres, or non-neuropathic, related to degenerative muscle or joint dysfunction [4]. Pain can also be caused by other MS symptoms and treatments [5]. Around a third of pwMS describe pain as one of their worst symptoms [4].

MS pain is treated predominantly from a biomedical approach. However, most pwMS only report some benefit from pain pharmacotherapies [6-8] and there is currently insufficient evidence to support their efficacy [9-11]. Offering pwMS an additional approach alongside medication for pain may be helpful.

There is preliminary evidence that adjunctive treatments for MS pain based on traditional Cognitive Behavioural Therapy (CBT) and Acceptance and Commitment Therapy (ACT) may be helpful in MS pain [12-15]. Treatment delivery methods in these studies have ranged from a half-day workshop to a ten week group programme. However, with the exception of one study [14], most were small and preliminary with little or no follow up, and all failed to examine

whether treatments were more or less helpful for people with varying disease courses or types of pain. A recent Cochrane review of two randomised controlled trials (RCTs) concluded that there is currently limited efficacy for CBT for neuropathic pain so more careful distinctions between effects on types of MS pain are warranted [16]. Furthermore, interventions evaluated have not been tailored according to a theory of pain in the context of MS. As this research is in an early stage more detailed analysis of individual responses to treatment may help tailor treatment specifically to the challenges of MS. A cognitive behavioural model of MS pain has been developed [17] based on a systematic review of MS pain, cognitive [18,19] and contextual-behavioural models of chronic pain [20], and the common-sense model of illness representations [21]. Our model was further refined based on qualitative interviews [22] and a large cross-sectional study ( $n=608$ ) investigating psychosocial correlates of MS pain severity and pain interference [6]. The model proposes that whilst disease factors trigger pain, a range of cognitive, emotional and behavioural responses may worsen its severity and interfere with daily functioning. Specifically, pwMS with greater pain severity and pain interference tend to view pain as serious, struggle in their attempts to control or reduce it, can be overwhelmed by pain, and avoid physical movement and social activities. Those who experience stronger negative emotional reactions to pain, perceiving it as chronic, uncontrollable, and as having serious consequences, also report poorer outcomes [6,17]. Pain and psychological processes may interact reciprocally, forming vicious cycles that worsen disability over time.

Most of the psychological processes identified in the MS pain model are amenable to change using either traditional CBT and ACT approaches for chronic pain [23,24]. Traditionally researchers have evaluated CBT or ACT approaches and their dominant underlying theories

independently. However, previous studies indicate that variables from both models explain important variance in pain outcomes, and it is unclear whether CBT or ACT would be a superior treatment [6,17]. Delivering ACT and CBT methods in combination may allow participants to exercise more choice in terms of using different techniques. CBT techniques may improve an individual's ability to problem-solve and enhance a sense of control, whilst ACT may address potentially unhelpful attempts to reduce or eliminate uncontrollable pain. No studies have combined CBT and ACT components in the context of MS pain, although a primary chronic pain study combining cognitive and contextual behavioural approaches showed significant improvements in outcomes [25].

When developing an intervention for MS consideration of how a treatment may be integrated within current services is important because access to psychological resources is often limited. There is growing evidence for the effectiveness of CBT for other MS symptoms, including fatigue and distress, and different methods of delivery have been evaluated [26]. Traditionally, CBT for pwMS has been delivered using high-intensity, face-to-face delivery methods [27,28], which can potentially be expensive and limit access to more disabled individuals [29]. Recently there has been a shift towards low-intensity self-management delivery methods in MS. One review suggests telephone- or internet-delivered self-management interventions for pwMS may improve access, clinical outcomes and quality of life, and reduce health care costs [30]. There is also evidence demonstrating that telephone support and web-based CBT interventions for MS fatigue are efficacious [31,32]. However, there are no published studies investigating the efficacy of a combined CBT and ACT self-management intervention for MS pain using these low-intensity delivery methods.

The purpose of the current preliminary study was to investigate the potential efficacy of a telephone-supported hybrid CBT and ACT self-management intervention for pwMS with pain based on our MS pain model [17] using mixed methods. Because MS is a heterogeneous condition, with substantial variability across individuals in terms of the extent of the symptoms and disability and nature of the pain, we opted for an in-depth case series method, to test how our broadly targeted treatment may work at an individual level for pwMS with a range of demographic and illness characteristics (i.e. disease subtype, level of neurological disability and type of pain) to provide a more detailed analysis of who may respond to the intervention. Specific aims were to (a) develop a pragmatic self-management focused intervention informed by the model, (b) assess potential changes in pain severity and pain interference across individuals, (c) evaluate individual psychological processes of change from our model, (d) explore pwMS' experiences of the treatment programme both in terms of acceptability and possible processes of change through post-intervention qualitative interviews and (e) inform recommendations for modifying the intervention in the future to inform the development of a larger RCT. In our model the strongest correlates of pain severity or pain interference included pain-related catastrophizing, acceptance, perceptions and negative emotional representations, and avoidance of social activities [6]. Therefore, these processes were specifically targeted in the intervention and measured as process variables.

## **Methods**

The study was approved by the Camden & Islington Research Ethics Committee London in December 2014 (14/LO/1909).

## Design

A replicated single-case time series A-B-A design with a four week baseline, eight week treatment and four week follow-up period.

## Participants

Participants, who agreed to be re-contacted about the current study, were recruited from a previous UK-wide cross-sectional study ( $n=608$ ) [6] based on their demographic and disease data. Specifically, the first author reviewed available cross-sectional survey data to purposefully select potentially eligible participants based on age, gender, ethnicity, MS subtype, level of neurological disability, pain severity and pain interference, pain onset and type of pain. Seven participants completed the intervention. Consistent with N-of-1 CONSORT reporting [33,34], figure 1 provides a full description of the flow of participants through the study.

**[Insert Figure 1 about here]**

### *Screening and eligibility criteria*

Participants completed a screening assessment, which included the Telephone Interview for Cognitive Status Modified (TICS-M) to assess capacity [35], and the following eligibility criteria:

Participants were included if they (a) had participated in our previous cross-sectional study, (b) were  $\geq 18$ -years of age with any MS subtype, (c) in line with chronic pain trial recommendations [36], experienced pain regularly for at least three months with a current pain severity and pain



interference score of  $\geq 3$  (moderate severity [37] assessed using the Brief Pain Inventory (BPI) [38], and (d) onset of pain occurred at the time of, or after, MS diagnosis.

Exclusion criteria were any of the following (a) non English speakers (b) reported previous serious psychiatric disorders, (c) severe cognitive impairment ( $\geq 20$  on the TICS-M), (d) starting on new pain medications or (e) psychological therapy for pain during the study period, and (f) prior experience of CBT or ACT.

As part of the eligibility assessment participants also completed the Self-administered Expanded Disability Status Scale (EDSS-S) [39] to assess neurological disability, MS subtype pictorials [40] and the Self-report Leeds Assessment of Neuropathic Symptoms and Signs pain scale (S-LANSS) [41]. The S-LANSS provided a case identification cut-off score ( $\geq 12$ ) to identify participants with neuropathic pain. The S-LANSS has good convergent validity with neuropathic items of the MS-validated Neuropathic Pain Scale [42]. Completers of the programme were given £80 for their participation.

### *Assessments*

All participants completed online self-report instruments assessing pain outcomes and psychological processes every four days during baseline (4 weeks), treatment (8 weeks) and follow-up (4 weeks). Whilst we acknowledge that pwMS pain levels are likely to fluctuate on a daily basis, the four-day interval for ratings, and shorter validated measures aimed to optimise validity, minimise participant burden, and limit the extent of missing data. The decision to use four-day ratings also confers with recent statistical methods, which allow for a smaller number of

data points per phase [43]. All measures demonstrated acceptable internal reliabilities in the previous cross-sectional study (Cronbach's  $\alpha \geq .80$ ) [6]. Three MS Society patient and public involvement (PPI) members provided feedback on the acceptability and usability of the online ratings. Every four days during the 16-week period participants were sent e-mail and text message reminders by an independent assessor (K.J.) asking them to complete their online ratings. At 12 weeks participants completed a semi-structured qualitative telephone interview with K.J., which explored their experience of the treatment programme (see Supplementary Table S1 for interview schedule).

## **Primary outcome measures**

### *Brief Pain Inventory Short Form (BPI).*

The BPI [38] is a valid and reliable measure of pain severity and interference instrument for pwMS [44]. The single-item pain severity 'pain now' scale, ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine"), and a modified 'general' pain interference scale for a given day, ranging from 0 ("does not interfere") to 10 ("completely interferes"), were used. Recent cut-offs for MS suggest an average pain severity score of 1 to 2=mild, 3 to 5=moderate, and 6 to 10=severe [37]. Guidance in chronic pain suggests a clinically meaningful change for pain severity reflects a 2-point shift in mean scores, whilst "substantial change" is 4, and "minimal change" 1 [45].

## **Secondary process measures**

### **Cognitive processes and thought patterns**

### *Pain Catastrophizing Scale (PCS)*

The PCS assesses the extent to which pwMS magnify or exaggerate the threat or seriousness of pain sensations [46]. The 13-item scale incorporates rumination, magnification and helplessness, with higher scores reflecting greater pain catastrophizing.

### *Brief Illness Perceptions Questionnaire (BIPQ)*

Four of the eight items from the BIPQ [47] were used to assess pwMS' perceived time-course, consequences, control and emotional representations of pain, by replacing the word "illness" with "MS-related pain".

## **Behaviours and behavioural processes**

### *Avoidance-Endurance Questionnaire Pain-related Behavioural Responses Scale (AEQ)*

The AEQ is a valid and reliable instrument assessing pain-related behaviours in response to chronic pain [48]. A modified version of the 6-item avoidance of social activities subscale (ASAS) was used to assess pwMS avoidance of social activities in response to pain on a given day. Higher average scores reflected greater levels of socially avoidant behaviour.

### *Chronic Pain Acceptance Questionnaire (CPAQ-8)*

The CPAQ-8 item scale assesses acceptance of pain, defined as the ability to open up to unwanted painful experiences and not struggle with them, when to do so serves one's goals [20].

Higher scores reflect greater acceptance of pain. The CPAQ-8 is validated in chronic pain populations [49,50]

## **Treatment**

The “Guided cognitive behavioural self-management Treatment for MS pain (GIFT)” manual was based on our empirically supported model of MS pain [6,17,22], mapping directly onto elements of traditional CBT and ACT for chronic pain [20,51,52] and MS fatigue [32,53]. The main aim was to help participants understand and develop new skills or strategies to address the biological, behavioural, cognitive, emotional and environmental factors that may contribute to, and maintain, MS pain. The manual was developed by the authors and incorporated feedback from three MS Society PPI members on the usability, usefulness and acceptability of information. The content of the eight sessions are summarised in table 1. All sessions were interactive and included self-assessments, task sheets, and a CD with optional audio exercises. This allowed the programme to be tailored to the individual’s unique problems, values-based goals, and progress through the programme. Participants could focus on aspects which they felt were relevant to them. Sessions included homework tasks, which were reviewed in subsequent sessions.

**[Insert table 1 about here]**

Participants also received three telephone sessions each lasting up to an hour. The first session, scheduled after participants completed chapter one, involved developing their personal five part model to inform the treatment rationale. The second session, delivered after chapter four,

explored the person's progress with values-based goals related to their model, which were monitored throughout the program. The final session focused on identifying thoughts, with the option of (i) challenging unhelpful thoughts or (ii) using cognitive defusion exercises, enhancing present moment awareness, and discussing strategies for dealing with setbacks. All sessions were collaborative in style, using Socratic questioning wherever possible. The sessions were delivered by A.H, a health psychology PhD student, who was guided by the content of the treatment manual. A.H. was supervised fortnightly by R.M.M, a registered health psychologist, and L.M., a lead consultant clinical psychologist for a chronic pain service. All sessions were audiotaped for fidelity checking and used for supervision.

## **Statistical analyses**

Time series data were plotted and visually inspected for each participant to explore differences in primary pain outcomes at pre-treatment (phase A), treatment (phase B), and follow-up (phase C). Whilst visual inspection of plots is recommended [54,55], recent studies show this method, and use of conventional statistics, can overestimate effects of interventions because time series data is autocorrelated [43,56]. Therefore, Simulation Modelling Analysis (SMA) software Version 8.8.3 [56] was used to generate effect sizes and autocorrelation (*AR*) adjusted p-values related to (a) the mean difference between baseline and intervention phase, and (b) rate of change in ratings from the start of treatment. In the current study 10000 resamples were conducted for each test. Pearson's *r* values were converted to Cohen's *d* to aid interpretation. Compared to other approaches for analysing time series data (see [43,57]), simulations indicate SMA protects against Type I error, whilst providing greater than 80% power to detect effects with 5 to 30 data

points per phase [43]. To explore if changes in pain were maintained, or continued to improve, at one month post-treatment, the same analyses compared baseline (phase A) and follow-up ratings (phase C).

All secondary psychological variables were visually plotted and the same phase- and slope-effect analyses were conducted using SMA. Overall, missing data across the sample was minimal (<0.01%), and dealt with using a last observation carried forwards imputation method. Finally, the post-treatment qualitative interview exploring pwMS' experiences of the programme were analysed by A.H. following established guidelines for inductive thematic analysis [58]. First, themes were derived for each individual, which were linked to their quantitative data, and themes common to all participants were then explored.

## Results

Characteristics of the seven participants at recruitment are shown in table 2, and pain medication use at pre-treatment and associated pain relief is presented in Table S2. Visual plots presenting all seven participants four-day BPI pain ratings during the 16 week period are summarised in figure 2, with corresponding SMA outputs in Supplementary Tables S3 and S4. The visual plots for the four-day ratings (z-scores) for the secondary psychological processes pain catastrophizing (PCS), pain acceptance (CPAQ-8) and avoidance of social activities (ASAS) for each participant over the 16-week period are presented in figure 3, with corresponding SMA outputs in Supplementary Tables S5 to S7. Perceptions and emotional representations of pain (BIPQ) are presented in figure 4 with statistical tests in Supplementary Tables S8 to S11. Interview data are summarised in table 3.

Three of the seven participants (1, 4 and 7) showed significant improvements in pain severity, pain interference and a number of the process variables, although these varied across individuals. Two reported unchanging pain scores (2 and 3) but positive changes in some of the process variables. Two of the seven participants showed worsening pain and no change on process variables (5 and 6). Data from each of these three groups will be presented in turn followed by a summary of group themes from the qualitative interviews.

**[Insert Figure 3 about here]**

*Participants with positive changes in pain outcomes and processes.*

Participant 1 had RRMS with neuropathic pain and reported decreases in both pain outcomes, with a large clinically and statistically significant phase change in pain severity and pain interference from baseline to treatment and follow-up after controlling for AR. She showed changes in several psychological processes in parallel with improvements in pain outcomes. She experienced mostly large significant reductions in pain catastrophizing, negative emotional representations, and perceived consequences and chronicity of pain when comparing baseline to treatment, and baseline to follow-up. However, she did not show a statistically significant change in pain acceptance, social avoidance or perceived control. The latter was inconsistent with her qualitative view that the intervention increased her sense of control over pain (see table 3).

Participant 4 had SPMS and non-neuropathic pain, and decided to reduce her pain medications at the start of treatment (day 36). She showed a clinically significant 2.3 mean reduction in pain

severity across phases, and significant slope change from baseline to treatment. However, phase comparisons were not statistically significant. She reported a 2.5 mean reduction in pain interference at the onset of treatment after baseline. This finding was significant for slope but not phase change. However, she showed clinically and statistically significant improvements in pain interference from baseline to follow-up. She also experienced large significant increases in pain acceptance, and reductions in pain catastrophizing, avoidance of social activities, negative emotional representations, and perceived pain as less chronic at follow-up. Consistent with these changes, she spoke about how pacing, prioritising goals, and mindfulness exercises helped her to manage angry thoughts and feelings. Whilst she perceived more serious consequences of pain from baseline to treatment, this non-significant trend reversed at follow-up. There was no change on perceived control.

Similarly, participant 7 with PPMS and neuropathic pain, showed only slope change decreases in pain severity from baseline to treatment and follow-up. However, she demonstrated large clinically and statistically significant improvements in pain interference from baseline to treatment, which were maintained at follow-up. In terms of process variables, she showed significant reductions in perceived consequences of pain and avoidance of social activities at follow-up. She experienced slope reductions in negative emotional representations, perceived chronicity and pain catastrophizing, and an increase in pain acceptance, from baseline to follow-up. There was no change on perceived control of pain. This was consistent with her view that mindfulness exercises and writing down thoughts stopped her from acting on thoughts, fears and anxieties about pain, helping her to focus on goals.



*Participants showing positive change on process variables but not pain outcomes.*

Two participants with RRMS and neuropathic pain (2 and 3) showed no statistically significant improvements in pain severity or pain interference during the 16 weeks. Both participants were employed, and found it challenging to “*play catch-up*” with programme tasks due to work.

Participant 2 showed a non-significant trend of improvement in pain interference at follow-up. He demonstrated large significant reductions in pain catastrophizing and negative emotional representations of pain, perceiving pain as less chronic and as having less serious consequences from baseline to treatment, and follow-up.. He also showed a significant increase in pain acceptance at follow-up. These data were consistent with his view that treatment had not improved his pain despite his efforts to change it, but had mostly “*changed his attitude*” (see table 3).

Participant 3’s pain severity and interference mean scores were mostly unchanged. She showed a small reduction in pain catastrophizing consistent with her statement that she no longer “*completely panics*” when experiencing pain (see table 3) and viewed pain as having less serious consequences during treatment, but this reversed at follow-up. She also viewed her pain as significantly less chronic from baseline to end of treatment, with small increases in pain acceptance at follow-up. In her interview she described re-engaging in valued activities despite pain, but also reported not using new skills when experiencing severe pain and greater avoidance of social activities at follow-up.

*Participants with worsening outcomes and no change on process variables.*

Participant 5 showed a non-significant increase in pain severity and interference of 1 to 2 points respectively. This person had PPMS and was severely disabled, experiencing several health problems during the programme, including severe trigeminal neuralgia. Consequently, his medication was increased in the first few weeks of treatment, and from day 24 it increased gradually over the following six weeks. He reported that although the programme kept his mind occupied, the increase of medication affected his concentration and fatigue, preventing him from “absorbing” some of the content in the GIFT booklet. At day 114 (follow-up) he was hospitalised with Pneumonia. His deteriorating health was consistent with his view that examples provided in the booklet were less relevant for someone of his level of disability (see table 3).

Participant 6 had SPMS and severe non-neuropathic pain. He also reported gradually worsening pain severity and pain interference from baseline to treatment, demonstrating a large significant increase in pain severity at follow-up. At day 66 he contacted the first author to report that he felt increasingly depressed and socially isolated, and was bed-bound despite experiencing a period of improvement with graded exercise in the previous week. On completing his final telephone session (day 80) he had only reached chapter 4 of the eight week programme, and did not attempt any of the cognitive strategies in later sessions. In contrast, all other participants completed both optional cognitive modules in the programme booklet.

In his interview, participant 6 reported experiencing complete control over his pain throughout the programme, despite having significantly worse pain outcomes. He felt he learned “*not to*

*battle with pain*” and was “*less frightened*”, but was shocked at how remote from his values he was (e.g. being creative), suggesting that a recurrent infection and fear of social disapproval undermined his motivation to work towards values-based goals. A risk assessment was conducted and he was referred to his GP to discuss further mood management.

**[Insert Figure 4 about here]**

### *Group Themes*

Three dominant themes were identified across participants (see table 3). First, many found setting values-based goals tapped motivation. Second, most emphasised that telephone sessions maintained their motivation. Third, many found the treatment booklets overwhelming and overcomplicated, suggesting a web-based version would be less daunting and more accessible, particularly for those with greater levels of disability. Whilst pain ratings only changed for 3/7 most found the programme beneficial and talked about therapeutic processes and techniques in an insightful way. However, the varied knowledge and skills described by participants suggests they focused on different aspects of the programme.

## **Discussion**

This small case series study aimed to provide a preliminary evaluation of the potential efficacy of an eight-week telephone supported pilot intervention (GIFT) based on CBT and ACT designed to reduce pain severity and pain interference in pwMS using mixed methods.

Psychological processes drawn from our MS pain model were also explored as potential mechanisms of change.

In relation to our primary outcomes, three of the seven participants (1, 4 and 7) showed statistical and clinically significant reductions in pain severity and, to a greater extent, pain interference after controlling for autocorrelation [45]. These findings were consistent with preliminary pilot studies evaluating cognitive and contextual behavioural interventions for MS pain [12,13,15]. The more robust improvements in pain interference at follow-up indicate that participants gradually became more competent in practising newly acquired skills, or found cognitive skills taught later in the programme additionally helpful.

Two of the seven participants (2 and 3) did not appear to benefit from the programme. However, these participants reported milder levels of disability and explained that balancing the programme with employment was challenging. Participant 2 also reported a much higher level of pain relief from medications at initial assessment compared to recent findings [6,8], suggesting his pain was already well managed.

Two participants (5 and 6) reported worse pain outcomes. Participant 5 had PPMS, was severely disabled, and his poorer outcomes may have stemmed from his declining health during the programme. Participant 6 reported periods of depression and demotivation related to recurrent health issues and feeling socially isolated. It is therefore possible his problems were too complex for a low intensity self-management intervention focusing solely on pain. The mixed findings in pain outcomes across the group are consistent with practice-based evaluations of

interdisciplinary chronic pain management programmes based on CBT, showing that between 1 in 3, and 1 in 7 (depending on the outcome measure), achieve clinically significant improvements at post-treatment and follow-up, whilst 1% to 2% of patients deteriorate [59].

With respect to secondary processes, improvements in pain were generally accompanied by improvements in measures defined as possible therapy processes, including pain catastrophizing, negative emotional representations of pain, beliefs about chronicity and negative consequences, avoidance of social activities and, to a lesser extent, pain acceptance. Pain catastrophizing was the most robust process of change. The reductions in pain catastrophizing appear to be consistent with a hybrid case series intervention combining graded *in vivo* exposure and Dialectical Behaviour Therapy for chronic pain [25], a systematic review of RCTs evaluating CBT for chronic pain [23], and trials showing pain catastrophizing is a significant mediator of outcome in both CBT or ACT treatments [60,61]. Similarly, the changes observed in social and physical avoidance, and pain perceptions, were consistent with mediators of change observed in CBT trials for chronic pain [62] and MS fatigue [63].

Only two participants showed significant increases in pain acceptance at follow-up. Several controlled and uncontrolled studies have shown that pain acceptance is an important predictor of outcomes, or significantly improves, after interdisciplinary ACT treatments for chronic pain [64-67]. In addition, two recent pilot RCTs have demonstrated significant increases in pain acceptance after an ACT intervention in both primary and specialist care [68,69], and pain acceptance has been shown to be a significant mediator of pain severity, pain interference and depression after an outpatient CBT-based treatment program [70]. Therefore, the current findings

may reflect the hybrid nature of GIFT and suggests enhancing the acceptance component of the programme may be beneficial.

Two participants reported large reductions in pain catastrophizing and perceived chronicity of pain in absence of any significant improvements in pain outcomes. Both these participants were working and reported pressure of time as an obstacle to engaging in the programme. More time and structured sessions may have allowed greater change in behavioural variables leading to greater benefits for pain.

Perceived control of pain is likely to tap self-efficacy [71], reflecting an important predictor of outcomes in traditional CBT for chronic pain [60,72,73]. However, whilst some pwMS' reported greater control in the interviews, perceived control measured by the BIPQ did not change for any participant. When considered in relation to the mixed findings for pain acceptance, this may highlight key differences in the way CBT and ACT address the problem of pain [20]. Traditional CBT encourages participants to set goals, sometimes related to symptom reduction, which may involve scheduling relaxation, rest or physical activity [52]. In contrast, ACT encourages the person to take an open and willing stance towards pain in order to pursue valued life activities and deemphasises the importance of pain reduction or control [51]. Therefore, whilst these approaches complement each other to an extent, our attempts to integrate them may have inadvertently conveyed conflicting aims around enhancing control and acceptance. From a practical perspective, developing skills in either strategy is likely to require regular practise. Whilst participants were given the option to try either strategy, learning techniques from both approaches may have limited opportunities for more targeted practise in either method.

Our final aim was to explore participant's views of the programme within a qualitative telephone interview. Individual themes were not entirely consistent with quantitative findings. Whilst all pwMS found the programme beneficial, only three reported significant improvements in pain outcomes, and five in psychological processes. Group themes tended to focus on delivery methods. Most participants described the treatment booklet as overwhelming and overcomplicated. Whilst, most individuals understood key concepts or techniques taught within the programme, limited time may have precluded learning of new skills. The majority of pwMS expressed a preference for a user-friendly web-based version of the treatment booklet. However, contact with the therapist during the programme was highlighted as an important in maintaining motivation.

Consistent with our MS pain model [6,17], there were no obvious patterns of improvement related to type of MS, neuropathic versus musculoskeletal pain or level of disability. Whilst these findings are preliminary, they suggest this approach may be helpful for both types of pain. Rather factors affecting negative outcomes appeared to be related to other complex consequences of illness (e.g. pneumonia, disease progression and depression).

## **Limitations**

This was a preliminary non-randomised single case series study which precludes definitive causal interpretation and is limited in reliability and generality until replicated and extended in more powered RCTs. Although single-case series use individuals as their own controls [74], the

non-randomised and the bi-phasic nature of this A-B-A design means that is unclear whether observed effects are a reflection of the intervention itself, attributable to non-specific treatment effects (e.g. therapist attention), or a combination of these. However, RCTs are at risk of aggregation bias, which assumes the average characteristics of a group apply to individuals [75]. Therefore, whilst not definitive, the current study does explore if, how, why and when the current intervention may be effective for particular individuals [43]. Self-report ratings, disease measures and interview responses may be susceptible to measurement, non-specific treatment or therapist effects, and exaggeration or under-reporting. Using group-validated scales may also reduce their reliability, and the neuropathic pain measure (S-LANSS) [41] is yet to be validated in the MS population, limiting interpretation of findings related to pain subtype. Finally, SMA is relatively new and several potential limitations have been highlighted (see [56,76]).

## **Treatment Implications and Conclusions**

Findings offer some preliminary support for a telephone-delivered guided self-management hybrid ACT and CBT intervention based on our model of MS pain [6]. Since participants highlighted the complexity of the intervention, it might be that giving pwMS more time to complete sessions will help them to practise key skills. Eight weeks may have been too short, particularly for those pwMS with busy work commitments who showed some change on process variables but not on outcome. Preliminary findings also suggest that pwMS with complex problems might not benefit from a low-intensity intervention, and greater therapist contact may be helpful. Since two people got worse, pre-treatment screening for complex social and health issues and depression may minimise adverse outcomes. In any case findings warrant further



Harrison, A. M., McCracken, L. M., Jones, K., Norton, S., & Moss-Morris, R. (2016). Using mixed methods case-series evaluation in the development of a guided self-management hybrid CBT and ACT intervention for multiple sclerosis pain. *Disability and rehabilitation*, epub. [10.1080/09638288.2016.1209580](https://doi.org/10.1080/09638288.2016.1209580)

investigation within a larger RCT. RCTs should test theoretically-guided mediators and moderators of treatment and outcome to better understand how they work, and for whom. Whilst our cross-sectional data [6] indicated variables from ACT and CBT explained important variance in pain outcomes, combining divergent approaches to promote choice may have inhibited mechanisms of action specific to each approach. Therefore, it may be helpful to evaluate CBT and ACT independently in MS pain, or provide tailored pathways for one or the other in a web-based programme.

### **Declaration of Interest**

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## Figure Legends

Figure 1 CONSORT diagram participant flow through study

Figure 2 Four-day pain severity and pain interference ratings (0–10) Brief Pain Inventory (BPI) at baseline, treatment, and follow-up for participants 1 to 7

Figure 3 Four-day ratings of Pain Catastrophizing (PCS), Pain Acceptance (CPAQ-8) and Avoidance of Social Activities (AEQ-ASAS) at baseline, treatment, and follow-up for participants 1 to 7 (Z-scores)

Figure 4 Four-day ratings (0–10) on the Pain Perceptions Questionnaire (BIPQ) at baseline, treatment, and follow-up for participants 1 to 7

**Table 1** Outline of the hybrid traditional cognitive and contextual behavioural guided self-help treatment manual

Chapters	Focus
1. MS Pain explained	<p>What is Multiple Sclerosis (MS) associated pain?</p> <p>A summary of gate control theory, including physiological explanations of different types of pain.</p> <p>Understanding the biological, cognitive, emotional, social/environmental factors triggers and how these can maintain pain.</p> <p>Developing a personal cognitive behavioural model.</p>
2. Breaking vicious cycles: patterns of rest and activity	<p>Levels of activity, rest, and pain are reviewed in relation to individual's models and / or vicious cycles. Information explains how patterns of rest and activity or over-activity affect the body and pain. The importance of consistency in activity and rest is emphasised, and benefits of moderate physical exercise suggested (activity scheduling and self-monitoring).</p>
3. The natural tendency to avoid unwanted pain and setting goals	<p>The natural tendency to experientially avoid pain and associated thoughts and feelings is discussed, along with acceptance-based metaphors and an optional audio exercise (<i>Observe, Breathe Open up</i>).</p> <p>A workability analysis of behaviour (i.e. short- and long-term consequences) is considered in relation to the person's model and vicious cycles.</p> <p>Setting goals related to either activity or avoidance is suggested, and choosing specific and achievable goals is emphasised.</p>
4. Doing what matters: Thinking about goals in relation to values.	<p>Thinking about underlying motivation by exploring the differences between values and goals.</p> <p>Identifying values, including the optional <i>Eightieth birthday</i> exercise, and linking to them to goals.</p> <p>Setting values-based goals.</p>
5. Identifying unhelpful thoughts.	<p>Explanation of how perceptions of events can influence a person's responses to pain.</p> <p>Identifying unhelpful thoughts and feelings and considering common traps or 'errors' in thinking.</p>

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|---|---|
| 6. <b>Option 1:</b> Using alternative thoughts                              | Explanation of how to weighing-up a ‘negative’ thought and learning how to consider possible alternatives to help with levels of distress and limit unhelpful behaviour.  |
| <b>Option 2:</b> Stepping back from pain and related thoughts and feelings. | The problems with suppressing pain, thoughts and feelings are discussed.<br><br>Defusion exercises are introduced ( <i>Lemons, lemons, lemons</i> and “ <i>I notice I’m having the thought that...</i> ”) to understand the potential influences of thoughts on behaviour, and to get distance from them without trying to change them.   |
| 7. Contacting the present moment.   | An explanation of the importance of getting present in order to be more open to pain and to pursue values-based goals.<br><br>Mindfulness exercises are introduced, including audio ( <i>Body Scan</i> ).   |
| 8. Preparing for the future.  | Developing a future management plan and setting long-term values-based goals with smaller objectives.<br><br>Exploring potential barriers and identifying physical or emotional warning signs of relapse and normalizing these.<br><br>Thinking about reconnecting with values and trying again to keep a commitment, or part of a commitment, to values-based goals.<br><br>Emphasis on continuing to employ the skills learnt throughout the manual to manage their pain. |
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**Table 2** Participant characteristics at recruitment

ID	Age	Gender	Ethnicity	Employment Status	MS Subtype <sup>1</sup>	Years Since Diagnosis	Neurological Disability (EDSS-S)	Pain Severity (BPI) <sup>2</sup>	Pain Interference (BPI)	Pain Location	Pain Subtype (S-LANSS) <sup>3</sup>	Pain Duration
1	42	Female	White-British	Retired	RRMS	20.54	6.5	8	7	Right torso, legs, eyes	14 (N)	2.58
2	37	Male	Mixed-White and Asian	Part time	RRMS	8	6	4	4	Hands, Legs	18 (N)	8
3	47	Female	White-British	Full time	RRMS	2.65	4.5	8	8	Feet, legs, face	24 (N)	2.58
4	45	Female	White-British	Unemployed	SPMS	23.55	6.5	8	5	Chest, legs, head	11 (NN)	2.91
5	45	Male	White-Scottish	Retired	PPMS	17.53	8	7	7	Feet, legs, hands, face	10 (NN)	14.61
6	65	Male	White-British	Retired	SPMS	19.03	7	4	4	Buttocks, feet, legs, arms	9 (NN)	11.8
7	56	Female	White-	Unemployed	PPMS	9	7	5	7	Chest, legs,	19	8.03

British

head, neck

(N)

ID: Participant identification number;

**Disease variables:** RRMS: relapsing remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis PPMS: primary progressive multiple sclerosis; EDSS-S: Self-report Expanded Disability Status Scale; S-LANSS: Self-report Leeds Assessment of Neuropathic Signs and Symptoms; N: neuropathic pain; NN: non-neuropathic pain.

**Pain outcomes:** BPI: Brief Pain Inventory Short Form on entering the study.

<sup>1</sup>Bamer et al's (2007) MS subtype pictorials with lay descriptions.

<sup>2</sup>All participants reported a pain severity score of 3 or greater, which according to recognised cut-offs (Alschuler, Jensen and Ehde, 2012) reflects pain of moderate to severe intensity.

<sup>3</sup>This is an approximation based on a self-report measure not yet validated in the MS population: A score of 12 or greater indicates pain of neuropathic origin (Bennett et al, 2005).



**Table 3** Key themes specific to individuals and the sample with examples

ID	Themes	Example Quotations
1	1. Getting over the initial, “Oh my god... there’s so much to do!”	<i>“There was quite a lot of information to read and understand, and I felt a bit overwhelmed in the beginning. Only because I was thinking, oh my god, there's so much to do and read and bits of tasks and things I needed to do.”</i>
	2. Goals were like mini projects	<i>“It was just like having a little mini-project to manage... I'd noticed that on a few days when I didn't get round to doing it [goals], for whatever reason, I could feel the difference. So it was then giving me the motivation to go back and start again... Let's get motivated again and let's get back on track.”</i>
	3. Practise makes natural	<i>“I probably think its [pain] changed because it was part of my goal-setting activity, and therefore when you do something and repeat it over and over, it just becomes part of your routine... One change would be certain things that I started out as having as goals have now been sort of slotted naturally into my life.”</i>
	4. Bringing self-worth and values to it	<i>“Also the other thing which came out very early on... probably in the first kind of phone call I had with [A.H.] was about self-worth and feeling valued. Because I'm no longer working he helped me to think about it differently and... coming at it from a different angle and somebody saying, actually, just because you're not working doesn't mean to say you can't bring a value to x, y or z.”</i>
	5. Human interaction kept me on track	<i>“The human interaction side of things... I think that was again a very useful thing. To have somebody to talk to at the start of the programme, and then towards the middle or the end of the programme. So that you knew what you were doing, what was expected and that you were on the track. Otherwise, I think I'm not sure how you would motivate people to stay on track.”</i>

6. Seeing reductions made me feel less anxious and more in control	<i>"I think it was a case of, oh actually there might be more to this than I first thought. I think, even if I can get my pain to be a four out of five most days, that has got to be a big upside to it being up to a nine some days and has me in tears. So I think noticing that I was less anxious about my pain levels... I felt that I'd gained a bit of control over it."</i>
2 1. Pushing yourself does not always mean worse pain	<i>"I used to be like oh if, it's like it said in the thing [booklet] if you overdo it, you think to yourself 'you are going to feel worse tomorrow' but it's not necessarily true really, the whole thing of don't overdo it, like I said and going to bed all the time, just saying, "You know what I am going to try and..." and it has been successful in a lot of ways."</i>
2. It's about changing your attitude	<i>"Like I said it's stuff that I thought about and tried anyway [strategies] without being like, oh I know it all, because I don't. It's just that I have realised myself that small changes in your attitude and not just thinking 'oh you know I am going to take my medicine and that is all I can do to deal with MS.' Because I think a lot with MS is your attitude... I think changes in mental attitude and just trying to look after your health, your mental health and your physical health, exercise and eating and stuff like that it makes such a difference and a lot of people need help with that I guess."</i>
3. It's been hard to keep up with things with work	<i>"It's been hard to keep up with things because it's been a lot more than I thought it would be, working as well full time, it's been difficult, but yeah I found it quite useful but, to me it's been more of just like, more of an attitude towards things rather than specific exercises itself... I have still yet to do the CD."</i>
4. You can't just do it with books can you?	<i>"I guess it's the type of person, it's the way that your mind works... I did have to discuss it [booklet] a little bit, you know working through the whole thing, this kind of programme you can't just do it with books really can you, it does have to involve a bit of talking."</i>

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5. Being told something different is motivating	<i>[A.H] would say to me try this week to do some of the things that you maybe would have given up on before. It's just nice to have somebody pushing you in a way. You know, it's like I said, say if I speak to my mum, she is always telling me to go to bed, just go to bed take it easy all the time, and it's just refreshing to speak to somebody and they say, you know what just try and do a few things and see how you feel, it's refreshing to have that kind of motivation."</i>
3 1. It stopped me falling back into negative cycles	<i>"I think it's helped me with the planning, it's helped with me, with my feelings towards the planning. It's helped me with my state of mind. It's helped me sort of find a way to approach doing those things without just feeling flattened by it afterwards and going back into one of those awful negative cyclical acts."</i>
2. I hadn't put it into words	<i>"The other thing I thought was really good was, as well as like giving, setting goals and tasks, was trying to identify the ways that you think. Because I knew that I was thinking in a very strange way and I knew I was behaving- I knew what was happening in this kind of negative cycle but I hadn't really identified, or I hadn't got the sort of titles to name those ways of thinking."</i>
3. Values-based goals are back on the radar	<i>"My exercise goals too - I really wanted to achieve that because that is part of my identity and very much linked-up with my values and the way I want to live my life... I think instead of my days just being about work and collapse, it feels like I've got work, and then I try quite hard to then fix on the other things."</i>
	<i>"You know there's a whole chapter on your values and making sure that your goals linked with your values - the ways that you live your life. That was a whole different way of looking at it for me. So, that's what I've tried to do. Bring in more of those things. So going to art galleries and going out into nature, seeing more friends that aren't local to where I live. Those are all part of my values."</i>
4. Mindfulness helped with goals	<i>"It's pretty dull being on an exercise bike. Trying to fill the time up with, like, quite often I think about my work or jobs I've got to do, so I almost</i>

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*start kind of reliving my work. So, I tried to stop doing that and tried to focus on my, you know my legs going round on the pedals, actually doing the sort of living in the moment of being on that exercise bike and listening to the outside sounds and enjoying that."*

5. Not completely panicking *"One thing is that doing the exercise does often make the pain worse initially. So I've tried to look at that and think, instead of just completely panicking, like I normally do, I've tried to think, OK [person's name], you know, I often use the words, well it was worth it."*

6. Changing the way you think and act in eight-weeks is challenging *"It is quite hard and it is quite a challenge to change the way that you think and the way that you act in eight weeks. I don't know why but labelling them and then trying to think in a different way - I found that enormously difficult, but I could do it. You know, that would be such an achievement, and I'm not saying I have, at all, but I'd like to."*

*"I tried to also include some ones [goals] that approached my sort of thinking. I've been less good at those. But what I've been quite good at is noticing when I'm doing it – although I'm not sure how good I've been at sort of putting them to one side."*

7. Playing catch up *"I had a lot of work building up in the middle of it and a [current job role] and, as I said to [A.H.], it would have been so easy to just stop because I just thought, oh my god, you know, when I get home I've got to do this, and I'm behind and the mad catch up!"*

8. When pain ramps up it's harder to apply *"I think that, you know, for me this course is absolutely fine when the pain is at one level. The second it sort of ramps up, that should be really the time that you imply this book, that you apply this book, isn't it? But somehow, when the pain increases, I find it harder and harder to stick to the book."*

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4 1. Encouragement with goals spurs you on *"He [A.H.] sort of encourages you and says, yeah, that's brilliant, we're on the right track. So, that spurs you on."*

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2. Pacing and prioritising helped with anger	<i>"I pace myself more... So if I've got more important things to get done, I get those done and not struggle on. So if I do lots and then I make myself tired, and I can't do the important things and then I get angry with myself, 'cause I haven't done them. So, it is making me pace myself more."</i>
3. Resting when in pain opens the gate	<i>"I've realised the difference of just being in [pain], and obviously it's really horrible. But if the pain is the predominant thing [then I find it helpful that I don't stop and just rest and do nothing because then I do focus on it and it makes me more anxious and that increases my pain - That opens the gate more [referring to Gate Control Theory].</i>
3. Putting it into words	<i>"Because I've always liked that, you know when other people put it in their words and it's sort of what you you've been thinking, or trying to put into words."</i>
4. Mindfulness helped me to let things go	<i>"On the CD, I liked the one on the river, the leaves on the river. I find that, I found that very, um, I've been doing that [a lot, because, 'cause I can just sort of let unhelpful things go, you know."</i>
5. Getting other's viewpoint	<i>"If there was something I found difficult, I'd go talk to my husband and he's very good. So it's quite good to have somebody else's viewpoint, isn't it? Somebody that knows you very well."</i>
6. Writing about your feelings was challenging	<i>"I sort of, I found they [task sheets] were hard. But it's just basically because it's writing about yourself, isn't it? A lot of it is your feelings and, I suppose, that, you don't really do that after school."</i>
5 1. Examples were rarely applicable	<i>"It is such a varied disease or condition, but I know you've got to cover all, so that's why maybe somebody who's less able than somebody else, maybe having more coverage for them."</i>

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| 2. Physical limitations with workbook | <i>"Some of the books were a bit awkward...The workbooks were probably the one thing that I had the most difficulty with. I think my [carer] did more on the workbooks than I did... I wanted to fill them in, but I just couldn't fill them in because they just, you know, about being able to get up and walk around."</i>   |
| 3. Skype® was personal                | <i>"Rather than see a telephone call, a telephone call just not would've been the same, whereas face-to-face, it's much better, you get a chance to meet the person, know what they're like and they get to know you as well. Uh, so I think the Skype idea is definitely one of the best things to do."</i>  |
| 4. It gave my brain something to do   | <i>"I was looking towards what's next session, you know? The next questionnaire, the next Skype call, I was always preparing for these things. So it's given me an, it's given me something to be more interested in. It's given me something to think about, use the old grey matter, which is starting to diminish quite a bit...So I used to work a lot and now I don't I feel I get quite lazy... This programme has given me something to think about and I'm now using my brain a lot more and I feel better for it."</i> |
| 5. Using distraction                  | <i>"Now if something does happen and I do get a bit of pain, then I automatically think back to the process that you're doing and try some of the exercises that [A.H.] gave me. You know, using my mind, trying to think of other things and things like that. It's certainly helping me... If you get a pain, it's too easy to just think oh, I've got a pain. I just can't keep my mind off it, whereas now I try and distract myself, think about other things."</i>  |
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| 6 | <p>1. Remoteness from values was shocking</p> <p>2. Fear of disapproval when working towards valued goals</p> <p>3. I learnt to absorb or accept pain and not fight it</p> <p>4. No man is an island (social isolation)</p> | <p><i>"Some were a bit shocking when you had to actually write them down. When you actually see them graphically, as plain as day in front of you it's- The quick exercise on values on page seventy-eight [values bulls-eye]... Work, education etc. each question I answered for leisure, relationships, personal growth, were right on the circumference. When you have the circle and you're trying to work your way into the centre of the circle, and graphically you see how far away from it you are."</i></p> <p><i>"I wanted to paint a lot but I don't want to do it because, I know this sounds crazy, but I won't do it because of my wife. Because of what she'd say, she'd tear me to shreds - I know she'd criticise whatever I did... that's the hardest bit, my wife coming and saying, what the hell are you doing that for? You know. That's what I've got to get over."</i></p> <p><i>"Try and live with it and absorb it... you can't fight it and I'm one of these people and I've lived with this all my life, I'm a bit of a bull at a gate and I get cross with myself. I try and fight things. It's the opposite you've got to do. It taught me to back-off and go the opposite way of what I normally do."</i></p> <p><i>"It teaches you to look into yourself. To accept pain and it's not finished. You know, life... it dominates you so much and you've got to-. You shouldn't fight it in the way I used to fight it. You've got to absorb it more and that's not to let it dominate you all the time."</i></p> <p><i>"It's rather like being on an island and you're a fish that's been thrown up onto this island out of the stream and everybody's in the stream and this island is circular and the river's going round and round this island. All your friends, your colleagues, everybody is swimming in the right race. You've been just thrown up onto the island and you can see them, and every now and then, they wave at you or they might hop on and say, "hello", but that's all and then they go back and swim. You know that you'll never join them and swim again. You will never be in that life again."</i></p> |
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5. Physical health problems can mean two steps back	<i>"I went into another urine infection on Sunday evening. They're terrible, I thought I'd had it for three years and it puts you into, virtually an epileptic fit and I had to wait until Monday morning before I got antibiotics... You are completely shattered, you know, you could be paralysed and then within five days you're almost- You've got back to where you were [referring to exercise-based goals]."</i>
7 1. Stopping myself act on thoughts and fears	<i>"I'm, sort of stopping myself from doing things, you know related to my thoughts, fears and anxieties... and it's has made me change my behaviours a lot."</i>
2. Mindfulness exercises helped ground anxiety and set goals	<i>"I found the leaves on a stream exercise very helpful, I've used that a lot, and I can use that without the CD now in my head, so I found that was very powerful, which is something that I will do when I've got a moment on my own. I will sit and use that to sort of bring me back down to where I should be if I'm starting to get anxious or trying to avoid pain or setting any goals. So I find that really helps me."</i>
3. Unhelpful thought records made me think "Crikey, is this me?"	<i>"The unhelpful thought record that I sort of had to keep around session five, I think having to write it down sort of made it hit home more what I was trying to achieve, you know, it was a situation as such. But in the end it actually helped me, but at the time I felt, you know I sat back and read it to myself and I thought, 'Crikey, is this me?' you know."</i>
4. A new romantic relationship and treatment helped	<i>"I'm feeling far more positive about life really, because I have met somebody new, and I do put part of that positivity down to the programme actually. It all sort of came at the same time, so I think it helped me. When I look back at it now, and you know, start reading the notes I've written, I can see that my life has improved since those few weeks ago, and I seem to be coping more with the pain and am more able to rise</i>



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*above it and lead a more normal life."*

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#### Themes across the sample

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| 1. Goals tapped motivation          | <i>"One of the ones [goals] is the exercise. I really wanted to achieve that because that is part of my identity and very much linked up with my values and the way I want to live my life."</i> (Participant 3, RRMS)   |
| 2. Human contact kept up motivation | <i>"Speaking to [A.H.], he sort of encourages you and says, 'yeah that's brilliant!' we're on the right track. So, that spurs you on."</i> (Participant 4, SPMS)<br><br><i>"Talking to someone that is just going to say, "Oh give it a go" it is more of an objective for you I suppose."</i> (Participant 2, RRMS) |
| 3. Create an online version please! | <i>"If the whole thing was on a website, you could just click onto the website and choose what you wanted to do. Or if you wanted to click onto links that were in the book. If that was all up on a one website it would be really useful."</i> (Participant 1, RRMS)   |
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Harrison, A. M., McCracken, L. M., Jones, K., Norton, S., & Moss-Morris, R. (2016). Using mixed methods case-series evaluation in the development of a guided self-management hybrid CBT and ACT intervention for multiple sclerosis pain. *Disability and rehabilitation*, epub. [10.1080/09638288.2016.1209580](https://doi.org/10.1080/09638288.2016.1209580)

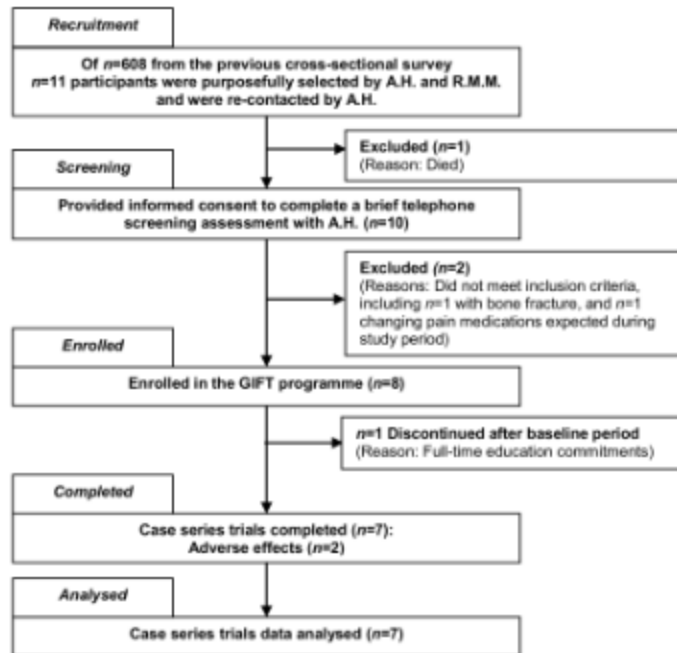


Figure 1

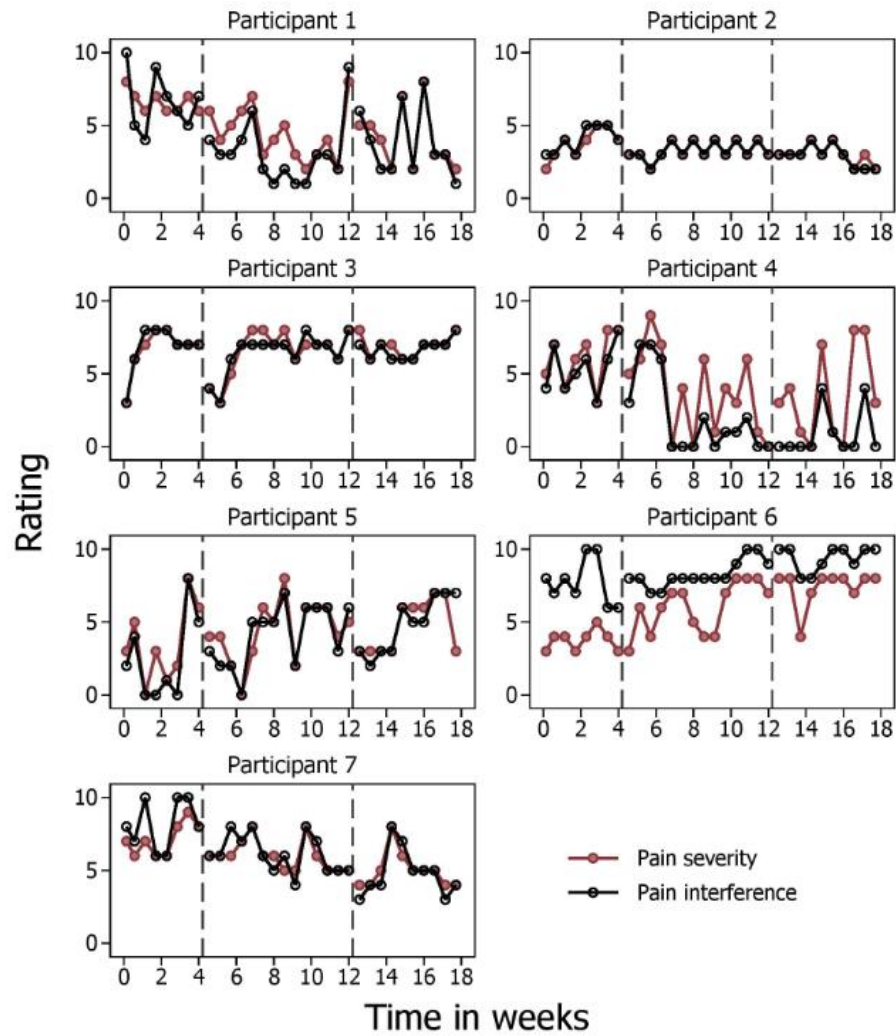


Figure 2

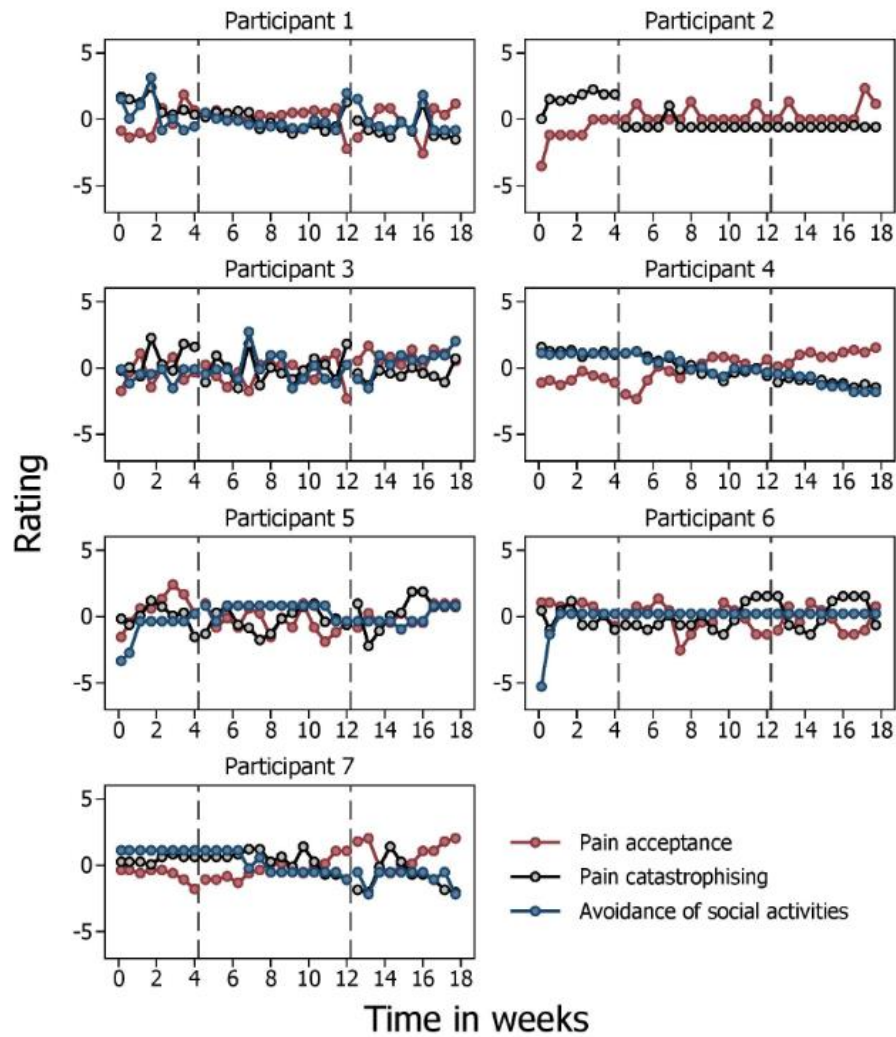


Figure 3